STN

FILE 'HOME' ENTERED AT 09:34:37 ON 22 AUG 2003

L1 71 (RSV OR (RESPIRATORY (A) SYNCYTIAL OR RS) (A) VIRUS) AND ATTENUA
T##### (P) (CIS-ACTING OR REGULATORY OR START OR STOP OR GENE-ST
ART OR GENE-STOP)

(FILE 'HOME' ENTERED AT 09:34:37 ON 22 AUG 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH' ENTERED AT 09:35:05 ON
22 AUG 2003

L1 71 S (RSV OR (RESPIRATORY (A) SYNCYTIAL OR RS) (A) VIRUS) AND ATTE
L2 30 DUP REM L1 (41 DUPLICATES REMOVED)
L3 8 S L2 NOT PY>1997

L3 ANSWER 1 OF 8 MEDLINE on STN
AN 97078805 MEDLINE
DN 97078805 PubMed ID: 8918930
TI Nucleotide sequence analysis of the **respiratory syncytial virus** subgroup A cold-passaged (cp) temperature sensitive (ts) cpts-248/404 live attenuated virus vaccine candidate.
AU Firestone C Y; Whitehead S S; Collins P L; Murphy B R; Crowe J E Jr
CS Laboratory of Infectious Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland 20892-0720, USA.
SO VIROLOGY, (1996 Nov 15) 225 (2) 419-22.
Journal code: 0110674. ISSN: 0042-6822.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-U63644
EM 199612
ED Entered STN: 19970128
Last Updated on STN: 19970128
Entered Medline: 19961231
AB The complete nucleotide sequence of the **RSV** cpts-248/404 live **attenuated** vaccine candidate was determined from cloned cDNA and was compared to that of the **RSV** A2/HEK7 wild-type, cold-passaged cp-**RSV**, and cpts-248 virus, which constitute the series of progenitor viruses. **RSV** cpts-248/404 is more **attenuated** and more temperature sensitive (ts) (shut-off temperature 36 degrees) than its cpts-248 parent virus (shut-off temperature 38 degrees) and is currently being evaluated in phase I clinical trials in humans. Our ultimate goal is to identify the genetic basis for the host range **attenuation** phenotype exhibited by cp-**RSV** (i.e., efficient replication in tissue culture but decreased replication in chimpanzees and humans) and for the ts and **attenuation** phenotypes of its chemically mutagenized derivatives, cpts-248 and cpts-248/404. Compared with its cpts-248 parent, the cpts-248/404 virus possesses an amino acid change in the polymerase (L) protein and a single nucleotide substitution in the M2 **gene start** sequence. In total, the cpts-248/404 mutant differs from its wild-type **RSV** A2/HEK7 progenitor in seven amino acids [four in the polymerase (L) protein, two in the fusion (F) glycoprotein, and one in the (N) nucleoprotein] and one nucleotide difference in the M2 **gene start** sequence. Heterogeneity at nucleotide position 4 (G or C, negative sense, compared to G in the **RSV** A2/HEK7 progenitor) in the leader region of vRNA developed during passage of the cpts-248/404 in tissue culture. Biologically cloned derivatives of **RSV** cpts-248/404 virus that differed at position 4 possessed the same level of temperature sensitivity and exhibited the same level of replication in the upper and lower respiratory tract of mice, suggesting that heterogeneity at this position is not clinically relevant. The determination of the nucleotide sequence of the cpts-248/404 virus will allow evaluation of the stability of the eight mutations that are associated with the **attenuation** phenotype during vaccine production and following replication in humans.

L3 ANSWER 2 OF 8 MEDLINE on STN
AN 96386548 MEDLINE
DN 96386548 PubMed ID: 8794298
TI Recovery of infectious **respiratory syncytial virus** expressing an additional, foreign gene.

AU Bukreyev A; Camargo E; Collins P L
CS Laboratory of Infectious Diseases, National Institute of Allergy and Infectious Diseases, Bethesda, Maryland 20892-0720, USA.
SO JOURNAL OF VIROLOGY, (1996 Oct) 70 (10) 6634-41.
Journal code: 0113724. ISSN: 0022-538X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199611
ED Entered STN: 19961219
Last Updated on STN: 19980206
Entered Medline: 19961122
AB A previous report described the recovery from cDNA of infectious recombinant **respiratory syncytial virus** (**RSV**) strain A2 (P. L. Collins, M. G. Hill, E. Camargo, H. Grosfeld, R. M. Chanock, and B. R. Murphy, Proc. Natl. Acad. Sci. USA, 92:11563-11567, 1995). Here, the system was used to construct recombinant **RSV** containing an additional gene encoding chloramphenicol acetyltransferase (CAT). The CAT coding sequence was flanked by **RSV**-specific **gene-start** and gene-end motifs, the transcription signals for the viral RNA-dependent RNA polymerase. The **RSV**-CAT chimeric transcription cassette was inserted into the region between the G and F genes of the complete cDNA-encoded positive-sense **RSV** antigenome, and infectious CAT-expressing recombinant **RSV** was recovered. Transcription of the inserted gene into the predicted subgenomic polyadenylated mRNA was demonstrated by Northern (RNA) blot hybridization analysis, and the encoded protein was detected by enzyme assay and by radioimmunoprecipitation. Quantitation of intracellular CAT, SH, G, and F mRNAs showed that the CAT mRNA was efficiently expressed and that the levels of the G and F mRNAs (which represent the genes on either side of the inserted CAT gene) were comparable to those expressed by a wild-type recombinant **RSV**. Consistent with this finding, the CAT-containing and wild-type viruses were very similar with regard to the levels of synthesis of the major viral proteins. Each of 25 **RSV** isolates obtained by plaque purification following eight serial passages expressed CAT, showing that the foreign gene was faithfully maintained in functional form. Analysis by reverse transcription and PCR did not reveal evidence of deletion of the foreign sequence. This finding demonstrated that the **RSV** genome can accept and maintain an increase in length of 762 nucleotides of foreign sequence and can be engineered to encode an additional, 11th mRNA. The presence of the additional gene resulted in a 10% decrease in plaque diameter and was associated with delay in virus growth and 20-fold decrease in virus yield in vitro. Thus, introduction of an additional gene into the **RSV** genome might represent a method of **attenuation**. The ability to express foreign genes by recombinant **RSV** has implications for basic studies as well as for the development of live recombinant vaccines.

L3 ANSWER 3 OF 8 MEDLINE on STN
AN 95266253 MEDLINE
DN 95266253 PubMed ID: 7747420
TI A cold-passaged, attenuated strain of human **respiratory syncytial virus** contains mutations in the F and L genes.
AU Connors M; Crowe J E Jr; Firestone C Y; Murphy B R; Collins P L
CS Respiratory Viruses Section, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland 20892, USA.
SO VIROLOGY, (1995 Apr 20) 208 (2) 478-84.
Journal code: 0110674. ISSN: 0042-6822.
CY United States

DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199506
ED Entered STN: 19950621
Last Updated on STN: 19950621
Entered Medline: 19950609
AB In previous studies, a mutant (cp-**RSV**) of the **RSV** A2 strain derived from 52 serial cold passages in bovine embryonic tissue culture was highly **attenuated** in seropositive adults and children but caused upper respiratory tract disease in seronegative infants. We investigated the genetic basis for this **attenuation** phenotype by comparing the complete genomic RNA sequence of this virus with the published sequence of strain A2 as well as with that of its unattenuated wild-type parent (HEK-7) virus. RNA was extracted from virions grown in tissue culture, reverse transcribed, amplified by the polymerase chain reaction (PCR), cloned, and sequenced. Changes from the published A2 wild-type sequence were confirmed on independently derived cDNA clones and by direct sequencing of PCR fragments. The HEK-7 parent virus was then analyzed at these positions by direct sequencing of PCR fragments. Fifteen nucleotide differences between the published A2 wild-type virus and cp-**RSV** were found. None appeared to involve **cis-acting** RNA sequences. Of the 15 nucleotide differences, only 1 occurred outside a translational open reading frame (ORF), and 2 which did occur within ORFs were silent at the amino acid level. The remaining 12 nucleotide differences encoded amino acid changes. All 3 of the mutations which were silent at the amino acid level, and 8 of the 12 which resulted in amino acid differences, were also present in the HEK-7 parent virus and therefore were not changes acquired during the cold passages. Thus, the remaining 4 nucleotide differences and the attendant 4 amino acid changes are associated with the **attenuation** phenotype of the cp-**RSV**. Two of the changes occur in the F gene and two in the L gene. These results confirm the previously described **RSV** genomic sequence, provide the first sequence of a live **attenuated RSV** vaccine strain, provide the first sequence of an **RSV** strain which has been evaluated in chimpanzees and humans, and indicate that **attenuation** in humans of a pneumovirus can be associated with a relatively small number of nucleotide and amino acid changes.

L3 ANSWER 4 OF 8 MEDLINE on STN
AN 93042283 MEDLINE
DN 93042283 PubMed ID: 1420579
TI Field trials on a live bovine **respiratory syncytial virus** vaccine in calves.
AU Kubota M; Fukuyama S; Takamura K; Izumida A; Kodama K
CS Division of Veterinary Microbiology, Kyoto Biken Laboratories, Inc., Japan.
SO JOURNAL OF VETERINARY MEDICAL SCIENCE, (1992 Oct) 54 (5) 957-62.
Journal code: 9105360. ISSN: 0916-7250.
CY Japan
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199212
ED Entered STN: 19930122
Last Updated on STN: 19930122
Entered Medline: 19921222
AB Field trials were carried out in calves using a live bovine respiratory syncytial (BRS) virus vaccine prepared from the **attenuated** BRS

virus, strain rs-52. Two hundred seventy-five and 353 calves were vaccinated intranasally and intramuscularly, respectively. No undesirable postvaccinal reactions were observed in the vaccinated calves. Of the serum neutralizing (SN) antibody negative calves 89.7% (26/29) and 92.8% (90/97) developed SN antibody 1 month after intranasal and intramuscular vaccination, respectively. Most of the calves having SN antibody titers of 1:1 or 1:2 at the time of vaccination showed a significant increase in SN antibody titer. About 70% and 90% of the calves vaccinated intranasally and intramuscularly, respectively, maintained SN antibody for 6 months after vaccination. In a field trial, a natural BRS virus infection occurred about 5 months after the **start** of the trial. Ten of the 16 unvaccinated control calves showed respiratory symptoms due to BRS virus infection. On the contrary, all of the 68 vaccinated calves exhibited no symptoms at all, indicating efficacy of the vaccine.

L3 ANSWER 5 OF 8 MEDLINE on STN
AN 92327836 MEDLINE
DN 92327836 PubMed ID: 1626423
TI Gene junction sequences of bovine **respiratory syncytial virus**.
AU Zamora M; Samal S K
CS Regional College of Veterinary Medicine, University of Maryland, College Park 20742.
SO VIRUS RESEARCH, (1992 Jun) 24 (1) 115-21.
Journal code: 8410979. ISSN: 0168-1702.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199208
ED Entered STN: 19920821
Last Updated on STN: 19920821
Entered Medline: 19920813
AB The nucleotide sequences of seven gene junctions (N-P, P-M, M-SH, SH-G, G-F, F-M2 and M2-L) of bovine **respiratory syncytial virus** (BRSV) strain A51908 were determined by dideoxynucleotide sequencing of cDNAs from polytranscript mRNAs and from genomic RNA. By comparison with the consensus sequences derived from human **respiratory syncytial virus** (HRSV) mRNAs, **gene-start** and gene-end sequences were found in all BRSV mRNAs. There was a perfect match between the BRSV and HRSV in all **gene-start** sequences, except for the sequence of the SH gene which contained one nucleotide difference compared to HRSV A2; and the **gene-start** sequence of the L gene, which was one nucleotide shorter than the corresponding sequence of HRSV. Analysis of the intergenic regions showed a high degree of divergence in the nucleotide sequence between BRSV and HRSV. However, the length of the nucleotides in the intergenic sequences was similar for a given gene junction. As in the case of HRSV, the M2 and L genes of BRSV overlap by 68 nucleotides, suggesting a similar transcription **attenuation** mechanism. The sequences of the overlap, corresponding to the 3' end of the L gene, were almost identical between BRSV and HRSV.

L3 ANSWER 6 OF 8 MEDLINE on STN
AN 91049438 MEDLINE
DN 91049438 PubMed ID: 2173259
TI Transactivation of the Rous sarcoma virus long terminal repeat promoter by Marek's disease virus.
AU Tieber V L; Zalinskis L L; Silva R F; Finkelstein A; Coussens P M
CS Department of Animal Science, Michigan State University, East Lansing 48824.

SO VIROLOGY, (1990 Dec) 179 (2) 719-27.
Journal code: 0110674. ISSN: 0042-6822.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199012
ED Entered STN: 19910208
Last Updated on STN: 19970203
Entered Medline: 19901221
AB Transient expression of chloramphenicol acetyltransferase (CAT) was used to study Marek's diseases virus (MDV)-mediated transactivation of the Rous sarcoma virus long terminal repeat (**RSV**-LTR) promoter. Cotransfection experiments in primary avian cells were conducted using MDV high-molecular-weight DNA and plasmid pRSVcat. Increased CAT activity, relative to controls, was consistently observed in the presence of MDV. Enhanced CAT activity, expressed via the **RSV**-LTR promoter, was strictly dependent on the presence of MDV DNA or virus, suggesting that activation of the **RSV**-LTR promoter was due to factors expressed in MDV-infected cells. Differences in transactivation efficiency were observed between various strains and the serotypes of MDV. In particular, high- and low-passage pairs of serotype 1 MDV showed marked differences in their ability to increase CAT activity in pRSVcat-transfected cells. **Attenuation** of viral pathogenicity and decreased expression of some cell surface glycoproteins occur in high-passage MDV strains. Decreased transactivation ability in these same strains suggests that continuous passage in culture and **attenuation** may perturb a **regulatory** mechanism operating by transcriptional control. In addition, transactivation of the **RSV**-LTR promoter suggests that increased incidence of avian leukosis following vaccination by MDV may be due to MDV-mediated transactivation of endogenous ALV proviral LTR promoters. MDV-mediated transactivation was not limited to the **RSV**-LTR promoter. Serotype 3 MDV (HVT) efficiently transactivated the herpes simplex virus (HSV) alpha 4 (ICP4) and beta-TK promoters as well as the human cytomegalovirus (hCMV) immediate early promoter.

L3 ANSWER 7 OF 8 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
AN 97:697875 SCISEARCH
GA The Genuine Article (R) Number: XW142
TI Ambisense gene expression from recombinant rabies virus: Random packaging of positive- and negative-strand ribonucleoprotein complexes into rabies virions
AU Finke S; Conzelmann K K (Reprint)
CS FED RES CTR VIRUS DIS ANIM, DEPT CLIN VIROL, PAUL EHRLICH STR 28, D-72076 TUBINGEN, GERMANY (Reprint); FED RES CTR VIRUS DIS ANIM, DEPT CLIN VIROL, D-72076 TUBINGEN, GERMANY
CYA GERMANY
SO JOURNAL OF VIROLOGY, (OCT 1997) Vol. 71, No. 10, pp. 7281-7288.
Publisher: AMER SOC MICROBIOLOGY, 1325 MASSACHUSETTS AVENUE, NW, WASHINGTON, DC 20005-4171.
ISSN: 0022-538X.
DT Article; Journal
FS LIFE
LA English
REC Reference Count: 43
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB We have recovered from cDNA a rabies virus (RV) containing identical, transcriptionally active promoters at its genome (negative-strand) and antigenome RNA and directing efficient expression of a chloramphenicol acetyltransferase (CAT) reporter gene from the antigenome. Transcription of the antigenome CAT gene was terminated by a modified RV gene junction

able to mediate transcription **stop** and polyadenylation but not reinitiation of downstream transcripts. While in standard RV-infected cells genome and antigenome RNAs mere present in a 49:1 ratio, the ambisense virus directed synthesis of equal amounts of genome and antigenome RNA (1:1). Total replicative synthesis was reduced by a factor of less than 2, revealing an unexpectedly high level of replication activity of the transcriptionally active promoter in the absence of the parental antigenome promoter. Successful packaging of ambisense ribonucleoprotein complexes (RNPs) into virions demonstrated that the parental 5' end of the RV genome RNA does not contain putative signals required for incorporation into virions. As determined both for standard RV and ambisense RV, virus particles contained genome and antigenome RNPs in the same ratios as those present in infected cells (49:1 and 1:1, respectively), indicating indiscriminate incorporation of RNPs independent of signals in the RNA. Ambisense expression of multiple foreign genes from RV vectors may circumvent problems with transcriptional **attenuation** of rhabdovirus housekeeping genes.

L3 ANSWER 8 OF 8 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
AN 97:398120 SCISEARCH
GA The Genuine Article (R) Number: WZ571
TI An infectious clone of human parainfluenza virus type 3
AU Hoffman M A; Banerjee A K (Reprint)
CS CLEVELAND CLIN FDN, RES INST, DEPT MOL BIOL, 9500 EUCLID AVE, NC2, CLEVELAND, OH 44195 (Reprint); CLEVELAND CLIN FDN, RES INST, DEPT MOL BIOL, CLEVELAND, OH 44195
CYA USA
SO JOURNAL OF VIROLOGY, (JUN 1997) Vol. 71, No. 6, pp. 4272-4277.
Publisher: AMER SOC MICROBIOLOGY, 1325 MASSACHUSETTS AVENUE, NW, WASHINGTON, DC 20005-4171.
ISSN: 0022-538X.
DT Article; Journal
FS LIFE
LA English
REC Reference Count: 39
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB A full length clone of the human parainfluenza virus type 3 (HPIV-3) genome (called pHPIV-3) was constructed, and recombinant, infectious HPIV-3 was generated by transfecting pHPIV-3 and support plasmids encoding the HPIV-3 NP, P, and L proteins into HeLa cells infected with a vaccinia virus recombinant which expresses T7 RNA polymerase. T7 RNA polymerase promoters on the transfected plasmids direct the synthesis of transcripts encoding the NP, P, and L proteins and a full-length, positive-sense copy of the HPIV-3 genome, Generation of virus was dependent on transfection of pHPIV-3 and the HPIV-3 P- and L-encoding plasmids. However, a plasmid encoding the NP protein was not required since NP was expressed from pHPIV-3. Recovered virus was neutralized by anti-HPIV-3 antisera and shown to contain specific base substitutions characteristic of pHPIV-3. Recombination was shown to occur during recovery, as viruses with two distinct genotypes and phenotypes were isolated, The ability to produce infectious HPIV-3 engineered to contain specific alterations within the HPIV-3 genes and **cis-acting** elements expedites the study of all aspects of the virus replication cycle. Additionally, analysis of mutations may lead to the identification of **attenuating** genotypes, a key step in the development of a live virus vaccine.

WEST Search History

DATE: Friday, August 22, 2003

Set Name side by side	Query	Hit Count	Set Name result set
	DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=OR		
L13	l11 and (virus or RSV).ab.	23	L13
	DB=USPT; PLUR=YES; OP=OR		
L12	5716821.pn.	1	L12
	DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=OR		
L11	l9 and L10	134	L11
L10	l6 and (cis-acting termination or gene-end or stop) same (codon sequence or polynucleotide or DNA)	552	L10
L9	L8 and (RSV or (respiratory adj syncytial or RS) adj virus) same (substitution or mutation or deletion or addition or insertion or modificiation or alteration)	134	L9
L8	l6 and (termination or gene-end or stop) same (codon sequence or polynucleotide or DNA)	523	L8
L7	L6 and l5	9	L7
L6	l1 and l3	631	L6
L5	(RSV or (RS or respiratory adj syncytial) adj virus) and (nucleocapsid or N) with protein same (phosphoprotein or P) with protein same (large adj polymerase or L) with protein same (RNA adj polymerase or polymerase adj elongation or M2-1 or M2(orf1) or m2orf1 or m2 adj orf-1)	55	L5
L4	(RSV or (RS or respiratory adj syncytial) adj virus) and (nucleocapsid or N) with protien same (phosphoprotein or P) with protien same (large adj polymerase or L) with protien same (RNA adj polymerase or polymerase adj elongation or M2-1 or M2(orf1) or m2orf1 or m2 adj orf-1)	0	L4
L3	(RSV or (RS or respiratory adj syncytial) adj virus) and (reduc$5 or ablat$5 or inhibit$5 or modulat$5) with (gene or protein) adj expression	2134	L3
L2	(RSV or (RS or respiratory adj syncytial) adj virus) and (nucleocapsid or N) same (phosphoprotein or P) same (large adj polymerase or L) same (RNA adj polymerase or polymerase adj elongation or M2-1 or M2(orf1) or m2orf1 or m2 adj orf-1)	90	L2
L1	(RSV or (respiratory adj syncytial or RS) adj virus) and (substitution or mutation or deletion or addition or insertion or modificiation or alteration) with (cis-acting or regulatory or gene-start or gene-stop or termination) same (gene or sequence or nucleic or polynucleotide or genome or antigenome)	1514	L1